

### **Remarks/Arguments**

Claims 1, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 are pending in the application. Claims 2, 3, 5-28, 37-41, 44-48, 63-65, 83, 86 and 87 were previously canceled. No amendments to the claims are made herein. Accordingly, no new matter has been added.

### **Formal Matters**

Applicants note the Examiner's statement that the Applicants' Amendments to the Specification, submitted on June 4, 2009, have not been entered as no reasons were provided for the amendments (*see* Office Action at pp. 2 and 11).

Applicants reiterated their request to enter the amendment and provided reasons for the amendment to the specification in their Response dated November 2, 2009. Specifically, Applicants previously noted that Table 1 in the instant published application, *i.e.*, U.S. Application No. 20040242548, includes several compounds annotated with the phrase "(?) indicates text missing or illegible when filed." The structures were correct in the application as originally filed. Therefore, Applicants provided Table 1 with each structure enlarged for clarity. As such, Applicants again request that the amendment to the specification, dated November 2, 2009, be entered into the record.

### **35 U.S.C. §103(a)**

Claims 1, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO01/19784 ("the '784 application") and U.S. Patent 7,045,507/WO02/072031 ("the '507 patent").

According to the Examiner, the '784 application describes structurally similar tetracycline compounds as those embraced by the instant claims (*see* Office Action at p. 5). The Examiner also stated that the '507 patent describes structurally similar tetracycline compounds as those embraced by the instant claims. *Id.* Thus, the Examiner concluded that the claimed compounds would have been *prima facie* obvious (*see* Office Action at pp. 5-6). Applicants further note the Examiner's statement that the instant claims differ from the cited references "in that they are of different generic scope" (*see* Office Action at p. 5). Applicants traverse the rejection.

A rejection under 35 U.S.C. § 103 requires the following analysis: "[t]he scope and content of the prior art are to be determined; differences between the prior art and the claims at

issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved” *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Then, “the examiner must provide evidence which as a whole shows that the legal determination sought to be proved (*i.e.*, the reference teachings establish a *prima facie* case of obviousness) is more probable than not” (MPEP § 2142).

In 2008, the Federal Circuit revisited the issue of obviousness in the context of chemical compounds in *Eisai Inc. v. Dr. Reddy’s Laboratories, Inc. and Teva Pharmaceuticals USA, Inc.* 533 F.3d 1353 (Fed. Cir. 2008). Addressing the third *Graham* factor (*i.e.*, the differences between the claimed invention and the prior art), the Court stated:

[T]he analysis ... often turns on the structural similarities and differences between the claimed compound and the prior art compounds. Obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (*i.e.* a lead compound) in a particular way to achieve the claimed compound. *Id.* at 1356-57 (citations omitted).

As the arguments set forth below show, the Examiner’s arguments with respect to the ‘784 application and the ‘507 patent, alone or in combination, do not provide a *prima facie* case of obviousness, at least because the cited references do not provide a reasonable expectation that the claimed compounds would successfully treat or prevent malaria.

The ‘784 application describes the treatment of various disorders including bacterial infections, such as those caused by *E. coli*, *S. aureus*, *S. warnerii*, and *E. hirae*. The Examiner has failed to show where the ‘784 application describes methods of treating or preventing the currently claimed diseases, namely malaria. As a result, one of ordinary skill would not reasonably expect that the compounds described by the ‘784 application could be used to effectively treat or prevent malaria.

Further, one of ordinary skill could not reasonably predict that the compounds described by the ‘784 application could be used to treat or prevent malaria. Such a prediction requires the use of improper hindsight, based upon the teachings of the instant specification. The ‘784 application does not mention malaria. There is no reason present in the Examiner’s statements regarding the ‘784 application to lead one to look to treat or prevent malaria with the compounds recited therein. Such teachings are only found in the instant specification.

There is no reason for one of ordinary skill to combine the ‘784 application and the ‘507 patent. Although the ‘784 application describes 7-substituted tetracycline compounds, there is no mention of the specific 7-heteroaryl substituted compounds described in the current claims

and no mention of malaria treatment or prevention. The '507 patent describes methods and compositions for increasing the antifungal activity of an antifungal agent. Thus, there is no reason to combine the '784 application and the '507 patent. Further, even if the '784 application and the '507 patent were combined, one would not arrive at the claimed invention.

The '507 patent fails to cure the deficiencies of the '784 application. As described above, the '507 patent describes methods and compositions for increasing the antifungal activity of an antifungal agent. The Examiner has failed to show where the '507 patent describes methods of treating or preventing malaria. As a result, one of ordinary skill would not reasonably expect that the compounds described by the '507 patent could be used to effectively treat or prevent malaria. Further, even if the '507 patent and the '784 application were combined, one would not arrive at the claimed invention.

Accordingly, Applicants request reconsideration and withdrawal of the rejection.

#### **Double Patenting**

Unspecified claims have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 165 and 184 of U.S. Application No. 10/853,635 (now U.S. Patent No. 7,595,309); claims 109 and 115 of copending U.S. Application No. 10/996,119; and claims 1-5 of copending U.S. Application No. 12/351,409.

As stated in Applicants' previous Responses filed on June 4, 2009, November 2, 2009 and February 9, 2010, Applicants note that U.S. Application No. 12/351,409 is not publicly accessible on the USPTO website. Furthermore, this application is not accessible on Private PAIR. In fact, U.S. Application No. 12/351,409 is not a copending application which is assigned to the assignee in the instant case, Paratek Pharmaceuticals, Inc. As such, Applicants request withdrawal of this provisional rejection.

With regard to U.S. Application No. 10/996,119, Applicants traverse the rejection. As currently amended, claim 109 of U.S. Application No. 10/996,119 is drawn to pharmaceutical compositions comprising a tetracycline compound useful for the treatment of multiple sclerosis or arthritis. (Applicants note that claim 115 of U.S. Application No. 10/996,119 is canceled and, thus, this rejection is moot with respect to this claim.) The currently pending claims are drawn to methods for the treatment of malaria and related methods. Applicants submit that one of skill in the art would not reasonably expect to treat malaria with a composition designed for the treatment of multiple sclerosis or arthritis as these diseases are entirely unrelated. *See*

arguments above with respect to the 35 U.S.C. 103(a) rejection. Thus, the subject matter described in the current claims is not obvious in view of claim 109 of U.S. Application No. 10/996,119. As such, Applicants request withdrawal of this provisional rejection.

With regard to U.S. Application No. 10/853,635 (now U.S. Patent No. 7,595,309), Applicants previously submitted a terminal disclaimer, filed on November 2, 2009.

Claims 1, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending U.S. Application No. 11/490,867.

Applicants traverse this provisional double patenting rejection. As stated in Applicants' previous Response filed on February 9, 2010, M.P.E.P. § 804 section I, subsection B1 provides as follows:

If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. If the ODP rejection is the only rejection remaining in the later-filed application, while the earlier-filed application is rejectable on other grounds, a terminal disclaimer must be required in the later-filed application before the rejection can be withdrawn.

The instant application was filed on October 24, 2003. The cited co-pending Application No. 11/490,867 was filed after October 24, 2003. Thus, the instant application is the earlier-filed application with respect to these applications. Accordingly, this provisional double patenting rejection should be withdrawn upon the favorable resolution of all other outstanding rejections.

Unspecified claims have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over copending U.S. Application Nos. 12/351,409; 10/921,580; 10/943,571; 10/996,119; 11/039,230; 11/348,608 and 11/490,867.

As described above, U.S. Application No. 12/351,409 is not a copending application assigned to the instant assignee, Paratek Pharmaceuticals, Inc. As such, Applicants request withdrawal of this provisional rejection.

With respect to U.S. Application No. 10/921,580, this application is abandoned. As such, Applicants request withdrawal of this provisional rejection.

With respect to U.S. Application Nos. 10/996,119 and 11/490,867, the arguments made above with respect to these applications are incorporated herein. As such, Applicants request withdrawal of these provisional rejections.

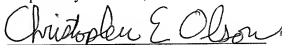
With respect to U.S. Application Nos. 11/039,230 and 11/348,608, Applicants recognize that the Examiner has noted Applicants' traversal of these provisional double patenting rejections in view of M.P.E.P. at § 804 section I, subsection B1 (*see* Final Office Action dated September 2, 2009 at p. 8). Accordingly, Applicants respectfully request withdrawal of these provisional double patenting rejections upon indication of allowable subject matter in the instant application.

With respect to U.S. Application No. 10/943,571, Applicants traverse the rejection. The currently pending claims of U.S. Application No. 10/943,571 are drawn to pharmaceutical compositions comprising a tetracycline compound useful for the treatment of disease associated with specific fungi. The instant claims are drawn to methods for the treatment of malaria and related methods. Applicants submit that it would not be obvious to treat malaria with a composition designed for the treatment of a disease associated with the specific fungi claimed in U.S. Application No. 10/943,571 as these diseases are entirely unrelated. *See* arguments above with respect to the 35 U.S.C. 103(a) rejection. Thus, one of skill in the art would not reasonably expect that the compositions described in U.S. Application No. 10/943,571 would successfully treat malaria. As such, Applicants request withdrawal of this provisional rejection.

**Conclusion**

Applicants submit that this paper is fully responsive and that the application is in condition for allowance. Should any questions arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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